Detecting fatigue from nocturnal heart rate variability

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ABSTRACT OF THE
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The focus of this thesis was to study if the level of fatigue could be assessed via nocturnal heart rate variability (HRV). HRV is a phenomenon that can be used to evaluate the status of the autonomic nervous system. A commonly used method for assessing the level of fatigue via HRV is an orthostatic test. The test is widely used by athletes in order to maintain the right balance between training and recovery. The test should be done every day as soon as possible after waking up, and therefore it may seem too laborious for nonprofessional athletes. Evaluating fatigue via nocturnal HRV would make monitoring fatigue less laborious by automating the measurement.

The data that was used in this study consisted of 234 overnight recordings of RRi (time interval between adjacent heart beats) and 234 orthostatic test from 11 different persons. The results of the orthostatic test were then compared to different HRV variables calculated from the nocturnal RRi measurements. The nocturnal HRV variables were calculated from two different segments from the RRi data.

The results reveal that the standard deviation of the RRi (std RRi) from the estimated slow-wave sleep (SWS) segment correlated with the mean RRi in the orthostatic test in standing position. The average correlation was minor ($\tau = 0.26 \pm 0.26$) and it was calculated with non-parametric Kendall's Tau test. Out of 11 participants, the correlation was statistically significant ($p < 0.05$) for eight participants.

It was concluded that the std RRi can not yet replace the orthostatic test in fatigue analysis. Despite the significant correlation, further analysis on the similarity of the std RRi and the orthostatic test should be conducted. Also due to interindividual differences, the suitability of this nocturnal parameter needs to be verified for each individual before one can consider leaving out the orthostatic test.

Keywords: heart rate variability, orthostatic test, fatigue, autonomic nervous system, sleep

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Tässä diplomityössä tutkittiin ihmisen rasituksen tason tunnistamista unenaikaisen sykevälivaihtelun (HRV) avulla. Sykevälivaihtelun avulla pyritään selvittämään autonomisen hermoston tila, joka puolestaan reagoi fyysiseen harjoitteluun ja siitä aiheutuvaan rasitukseen. Rasitusta arvioidaan ortostaattisen sykevälivaihtelutestin avulla, joka on erityisesti urheilijoiden käytössä. Ortostaattinen testi tulisi suorittaa päivittäin, aamulla heti heräämisen jälkeen. Tämän vuoksi se voi tuntua työläältä. Unen aikana tehtävä automaattinen rasittuneisuuden mittaus voisi helpottaa oman rasituksen tason seurantaa.

Tutkimuksessa käytetty aineisto koostui 234:stä ortostaattisesta testistä ja yhtä monesta läpi yön kestäneestä RRi (peräkkäisten sydämen lyöntien välinen aika) mittauksesta. Aineisto oli kerätty 11:ltä eri ihmiseltä. Unenaikaset sykevälivaihtelumuuttujat laskettiin kahdella erilaisella aikaikkunalla. Rasituksen arviointia unenaikasesta sykevälivaihtelusta tutkittiin vertaamalla unenaikaista sykeväliviahtelua ortostaattisen testin tuloksiin. Vertailu tehtiin laskemalla korrelaatio yksittäisen henkilön unenaikasen sykevälivaihtelun ja ortostaattisen testin tuloksien välille.

Voimakkain korrelaatio löydettiin arvioidun syvänunenaikaisen aikaikkunan (SWS segment) RRi:n keskihajonnan ja ortostaattisen testin seisomavaiheen keskimääräisen RRi:n välillä. Korrelaatio laskettiin parametrittomalla Kendallin Tau testillä ja keskimäärin se oli pieni ($\tau = 0.26 \pm 0.26$). Käytössä olleen data-aineiston 11 osallistujasta kahdeksalla tämä korrelaatio oli kuitenkin tilastollisesti merkittävä ($p < 0.05$).

Unenaikasen RRi:n keskihajonta ei sellaisenaan sovellu korvaamaan ortostaattista testiä. Lisätutkimusta unenaikaisen RRi:n keskihajonnan käyttäytymisestä suhteessa ortostaattisen testin tuloksiin tarvitaan. Lisäksi suurien yksilöiden välisten erojen vuoksi, unenaikasen RRin: keskihajonnan sopivuus tulisi varmistaa yksilökohtaisesti.

Avainsanat: sykevälivaihtelu, ortostaattinen testi, rasitus, autonominen hermosto, uni

Contents

Abbreviations

AV node	Atrio ventricular node
BMI	Body mass index ($\frac{kg}{m^2}$)
F-OR	Functional overreaching
HR	heart rate
HRV	heart rate variability
HF	High frequency band (0.15–0.4 Hz)
HFP	High frequency power (ms^2)
LF	Low frequency band (0.04–0.15 Hz)
LFP	High frequency power (ms^2)
MET	Metabolic equivalent
nF-OR	Non-functional overreaching
NREM	Non-rapid eye movement sleep. Sleep stages 1–4
OTS	Overtraining syndrome
pNN50	The proportion of consecutive RR intervals with more than 50 ms difference
PNS	Parasympathetic nervous system
REM	Rapid eye movement sleep
RMSSD	Root mean square of successive difference
RRi	Time interval between adjacent R peaks (heart beats)
rRR	Interbeat autocorrelation coefficient
RSA	Respiratory sinus arrhythmia
SA node	Sino-atrial node
SE	Sleep efficiency
SOL	Sleep onset latency
SNS	Sympathetic nervous system
std	Standard deviation
SWS	Slow-wave sleep
VO_2max	Maximal oxygen uptake, ($\frac{mL}{(kg*min)}$)
VT	Ventilatory threshold

1 Introduction

Well-being and health are values pursued by many. An essential piece in that puzzle is physical exercise. The health benefits of physical exercise are both physiological and psychological. Unfortunately, the coin always has the other side: in addition to the health benefits, physical exercise can also cause fatigue.

It is very important to have recovery and exercise in balance. Maintaining this balance is not easy. Even many professional athletes occasionally fail in this and end up training too hard [1]. Despite the heavy training, one's performance may start decreasing [2]. In general, this is called fatigue [3] (fig. 1). Fatigue can be caused by training or psycho-emotional factors such as work stress or lack of sleep [3, 4]. When fatigue has accumulated long enough, a person can be diagnosed with overtraining syndrome that is linked to adrenaline insufficiency [4]. Considering the ongoing fitness boom [5], studying fatigue and ways to detect it, seems very timely. In this study, the focus is mainly on training-induced fatigue.

Physical exercise challenges internal structures that try to maintain stable conditions. Autonomic nervous system (ANS) is one of the key players maintaining this balance called homeostasis. Physical exercise is an indirect way to affect the activity of the ANS. For example, increased heart rate (HR) during an exercise is caused by changes in the activity of the cardiac modulation by the ANS. Changes in the HR are modulated by changes in the ANS activity.

Heart is a muscle that keeps the blood circulating by contracting. This contraction is caused by changes in electrical potential of the heart muscle that can be measured from the skin surface. This technique of measuring the electrical potential changes of the heart is called electrocardiography (ECG). Heart beats are then detected from the ECG signal.

The human heart does not beat in a metronome accuracy [6]. This variation in the time intervals between heart beats is called heart rate variability (HRV). This variation originates from the autonomic nervous system. The magnitude of the HRV phenomena is generally considered as a marker of the ANS activity [7, 8]. The HRV phenomena can be interpreted in a different way by using different calculation techniques. For example, by calculating the root mean square of the successive difference of the time intervals between adjacent heart beats (RMSSD), magnitude of the RMSSD is caused mainly by the parasympathetic part of the ANS [9].

Sleep offers a stable environment for analyzing the HRV, as movement artifact and conscious processes do not affect the measurement. With successful fatigue monitoring, it could be possible to prevent overtraining. Fatigue monitoring would help people to maximize the health benefits and minimize the risks of training.

The goal of this study was to explore the possibilities of detecting fatigue from nocturnal RRi measurement. The main hypothesis is that fatigue could be detected by analyzing HRV during sleep. The nocturnal HRV was analyzed from two different segments. The hypothesis was tested by comparing the nocturnal HRV to the HRV variables calculated from an orthostatic test which a common method of evaluating the ANS activity.

A previously collected dataset was used in this study. The dataset included

234 nocturnal RRi recordings and 234 orthostatic tests recordings from 11 persons. The most common HRV variables and two novel ones were calculated from these recordings. The correlation between these variables was then studied. The research methods and materials are described in more detail in section 3.

2 Review of the literature

2.1 Physical exercise

There is no doubt of the health benefits of physical exercise. It can improve one's ability to handle stress, enforce bones and protect from cardiovascular diseases, to name a few [10]. Regular aerobic exercise is even known to decrease the risk of mortality [11]. These health benefits are related to changes in the internal functions of a body. For example, during exercise heart rate (HR) increases as a result of changes in the autonomic nervous system [11]. To achieve these benefits, exercise needs to be regular, preferably a way of life rather than just a regimen [10].

Body is constantly trying to maintain internal balance (homeostasis) and adapt to the environment. Training can be seen as a way to affect this adaptation. In general, the desired adaptive response from training is called supercompensation [12], (fig. 1). If recovery is not sufficient and training is too hard, no supercompensation will occur. This output of training and recovery is called training adaptation. It can be either positive or negative. Positive training adaptation means that your performance has improved (supercompensation), whereas negative adaptation can be defined as performance decrement despite the training. Training adaptation is typically evaluated in longer time scales rather than after individual exercise sessions.

In modern research, the state of the autonomic nervous system is assessed via analyzing changes in cardiac behaviour (i.e. heart rate variation) [6]. Training adaptation is noted to be individual variable. Not everyone reaches the same results with the same training program [11]. Therefore evaluating the effects of acute and regular exercises to autonomic functions may be helpful when designing individual training programs as suggested in [11].

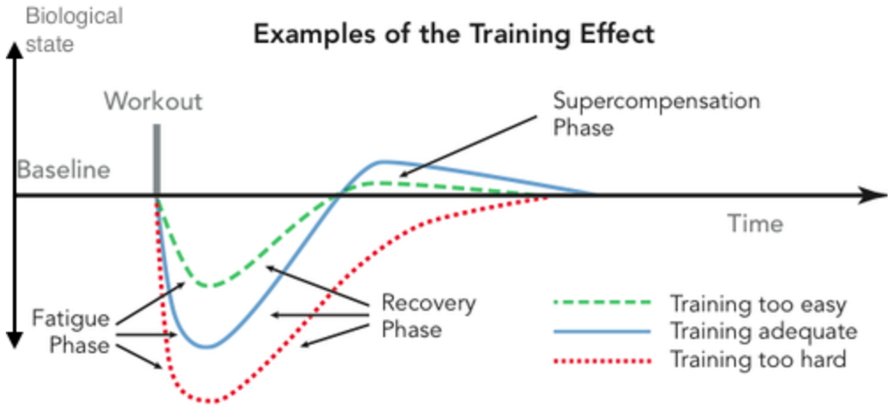

Figure 1: Principles of supercompensation training, modified from [13]. The blue curve represents the F-OR with desired super-compensations afterwards. The red curve represents non-functional overtraining with no supercompensation.

Overtraining

Overtraining is a common mistake among athletes. Overtraining is divided into three subcategories based on the severity of the state: overtraining syndrome (OTS), functional overreaching (F-OR, blue curve in fig.1) and nonfunctional overreaching (nF-OR, red curve in fig.1). OTS is the most severe of these forms of fatigue. The classification is done based on genesis and recovery time from the state. Overreaching is generated by the disproportion between rest and physical exercise. Functional overreaching is a state worth achieving due to possible supercompensation after the recovery. [2] The diagnosis of OTS, nF-OR and F-OR is rather complicated. Performance decrement and perceived experience are variables to look at, but retrospectivity of these make it complicated [2, 14]. In other words, overtraining is easiest to diagnose when it is already too late. Overtraining terminology with symptoms and recovery times is clarified in table 1.

Overtraining syndrome is further divided into two subclasses based on the origin of the syndrome: Addison (vagal) type OTS and sympathetic OTS [15]. The key factor for developing both of these forms of OTS is the long-term imbalance between training and recovery [15]. The generation of Addison type OTS is more related to high training volume whereas sympathetic OTS is more related to too high training intensity and other stressors like too many competitions and psychological stress [15]. The symptoms of Addison type OTS are very similar to adrenaline insufficiency [15].

Table 1: Overtraining terminology. Modified from [2]; [14]

State	**Definition**	**Recovery time**	**Results**
Functional overreaching	Temporary decrement of performance due to increased training	Days to weeks	Performance increases after rest (supercompensation)
Non-functional overreaching	Longer decrement of performance due to intense training. Full recovery can be achieved with rest. Can be accompanied by psychological symptoms.	Weeks to months	No supercompensation. A significant amount of training time will be lost due to long recovery
Overtraining syndrome	Generated like non-functional overreaching. Performance decrement typically last more than two months. More severe symptoms and longer recovery time.	Months	Negative outcome due to severe symptoms and long recovery time

Diagnosing overtraining

The diagnosis of overtraining and overreachings is rather complicated. There is no direct variable to describe the state of overtraining. The American College of Sport Medicine and the European College of Sport Medicine agreed that the main markers of OTS are performance decline, mood changes and general fatigue [14].

Biomarkers widely used in overtraining studies are urea, urin acid, ammonia and creatine kinase [2]. Those markers are not easily utilized independently in a home environment.

2.2 Sleep

Consciousness is divided into three different levels: awake, rapid eye movement (REM) sleep and non rapid eye movement (NREM) sleep. NREM sleep can be divided further on into stages s1–s4. REM sleep is characterized by rapid eye movements and low-voltage activity in the brain. The electrical brain activity in REM sleep is very close to awake state, but there is no tension in muscles [16, p.5].

The deepest sleep phases, NREM stage 3 and NREM stage 4 are called slow-wave sleep (SWS) or synchronized sleep. The latter name comes from the functionality of cortical nerve cells. When awake, cortical nerves are functioning individually, but they begin to synchronize with each other as alertness approaches SWS. The SWS is generally considered the most recovering sleep. Growth hormone can be excreted in relatively large doses during slow-wave sleep. Adequate sleep is therefore very important for the growth of children and adolescents. Blood pressure is known to decrease and respiratory rhythm is known to be stable during SWS. There is relatively more SWS in the early night, and the amount and length of REM sleep phases increase towards morning. [17, p. 234]; [16, p. 5].

A healthy normal sleeper experiences different sleep phases in a cyclical manner [16, p.5]. An average length of a sleep cycle is approximately 90 minutes [17, p.234], but it varies with age. The general trend is that the need for sleep decreases with age [16, p. 5–6]; [18, ch. 11].

Sleep is usually presented in a two-dimensional graph, where the level of consciousness is presented as a function of time. This graph is called hypnogram. The high values in hypnogram represent a high level of consciousness and vice versa. See figure 2 for an example of a hypnogram.

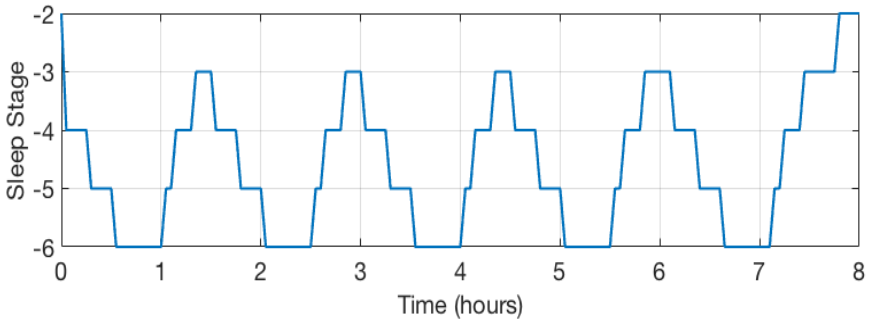

Figure 2: Hypnogram presenting sleep phases and sleep cycles. Y axis is labelled with following indices: awake = -2, REM = -3, NREM stage 1 = -4, NREM stage 2 = -5, NREM stages 3 & 4 = -6

2.2.1 Exercise affecting sleep

There is a two-way connection between sleep and exercise. In the ideal case they support each other, but in the worst case, they can disturb each other. In order to maintain and promote health one should perform 30 min of moderate-intensity aerobic activity five days a week, or 20 min of vigorous-intensity activity in three days a week [19]. The intensity of physical activity can be presented in Metabolic equivalents (MET). MET number tells the amount of increased energy consumption compared to resting energy consumption. For example, a vigorous-intensity activity of seven METs consumes seven times more energy compared to restful sitting. Vigorous-intensity activity is defined to be above six METs i.e. running for example. Moderate intensity activity is defined to reach from three to six metabolic equivalents (METs). A good example of such moderate intensity activity would be walking fast. [20]

Some studies on sedentary women report finding of the connection between acute physical exercise and sleep. It was found that if the exercise was performed 4–8 hours before bedtime, the latency of falling asleep was shorter and there was less wake after falling asleep. The exercise was found to have an influence on the structure of the sleep. After the exercise, the amount of REM sleep decreased and there was a minor increment in the amount of SWS and in the time before the first REM phase. [19]

Functional overreaching has been found to have an influence on sleep. Athletes detected with F-OR had significantly decreased sleep efficiency (SE), sleep duration and immobile time. It is not completely sure whether these decrements in sleep were symptoms of F-OR or whether sleep decrements caused F-OR. [21].

Sleep onset latency was found to be decreased due to regular exercise. Regular exercise was also detected to increase the total sleep time, sleep efficiency and REM sleep latency [22]. These increments in sleep are nearly the opposite of what was found with F-OR athletes. The sleep improvements caused by regular training [22], are consistent with previous research [19]. The effects of regular exercise to sleep are not unambiguous. It induces many significant improvements in cardiac functions and basic metabolic rate, for example. This is why it is hard to draw a clear line between direct and indirect effect of exercise to sleep. [19]

It may then be concluded that in terms of sleep, exercise is recommended at any time of the day, as long as it does not decrease one's sleeping duration. This conclusion is well in line with the recommendations of The National Sleep Foundation. [19]

2.2.2 Sleep restrictions and physiological performance

People are not very good at evaluating the effects of sleep loss [23]. Especially professional athletes who do not always have the optimal conditions for sleeping should pay attention to their sleep quality. The efficacy of exercise is dependent on many factors such as biomechanics, psychology and physiology and the effect of sleep deprivation on these is not well known [19]. A recent study among Taekwondo practitioners showed that lack of sleep decreased the performance in a Yo-Yo intermitten recovery test [24]. The most harmful to the performance was if the sleep was limited at the end of the night (i.e. waking up too early). No changes in peak heart rate were found after limiting the sleep at the end of the night [24]. Full deprivation was also found to be harmful for exercise performance. In a timed running distance test the participants ran covered less distance after deprived night [25]; [26]. Despite the results in the running test, sleep deprivation did not cause any significant difference in pre–exercise cardiorespiratory parameters [26]. Among athletes who were training high accuracy sports such as tennis or darts, the negative effects of sleep deprivation were even greater [23].

The figure 3 summarizes the findings from the connections between sleep and exercise.

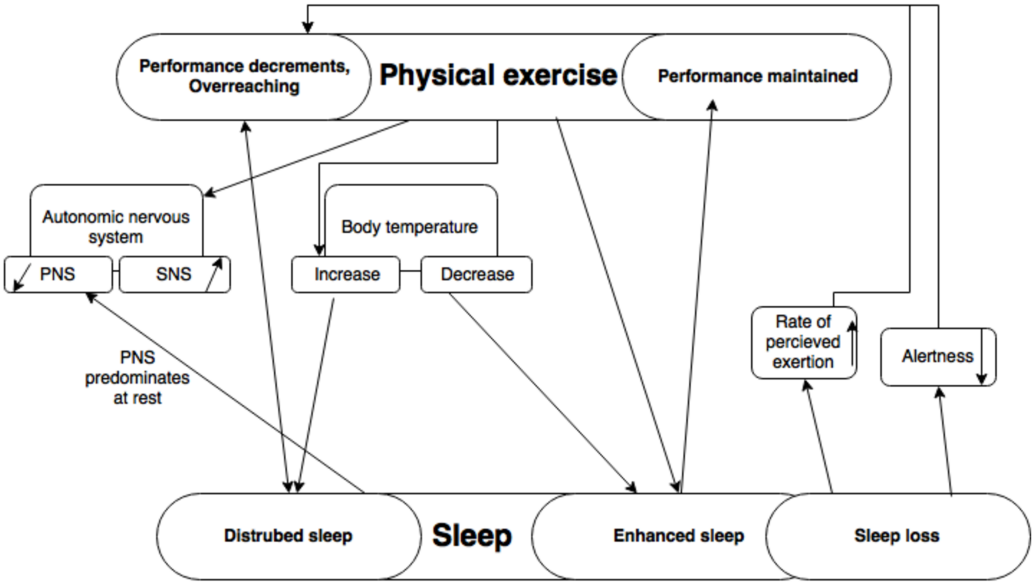

Figure 3: Interactions between sleep and exercise. PNS = parasympathetic nervous system activity, SNS = sympathetic nervous system activity modulation. Modified from [19].

2.3 Physiology of the heart

Human heart is a hollow muscle. It weights approximately 300–500 grams. It is an absolutely vital organ that keeps the blood circulating and ensures the transportation of oxygen and nutrients.One of the specialties of the heart muscle (myocardium) is that it is nearly tireless. The number of beats per lifetime is enormous. It can be even up to three milliard. [17, p. 318–321]

The heart consists of left and right half. The halves are further divided into ventricles and atrium. The atrias are the input channels and ventricles are the output channels of the heart for circulating blood. The core of a functioning heart is its ability to contract, i.e pump blood. [17, p. 318–321]

ECG & Myocardium

The contraction of the heart muscle is caused by changes in the electrical potential of the heart muscle. This electrical potential can be measured from the skin surface with a technique called electrocardiography (ECG). The ECG measurements are usually presented in a graph where the voltage is plotted as a function of time. A voltage curve of a single cardiac cycle presented in figure 4. Cardiac ECG cycle consists of P wave, QRS complex and T wave [27, p. 451–454]. P wave is produced by depolarization (excitation) of the atriums. The QRS complex is formed by ventricle depolarization. T wave is formed by ventricle repolarization where the electrical potential recovers back to the resting potential. [17, p. 320–321].

Circulatory system

The blood circulation is the main task of the cardiovascular system. The system consists of the heart and the circulatory system (i.e. vascular system). The circulatory system can further on be divided into pulmonary and systemic circulation. [27, p. 439–440]

Pulmonary system is responsible for transporting blood from the right side of the

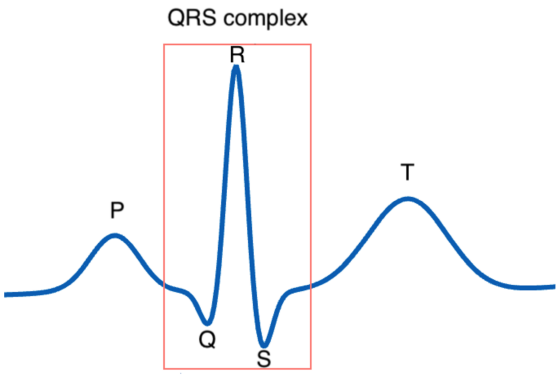

Figure 4: P wave, QRS complex and T wave form a complete cardiac ECG cycle. The voltage is presented as a function of time.

heart to the lungs and further on to the left side of the heart. Systemic circulation in turn, is responsible for delivering oxygenated blood all over the body and for returning deoxygenated blood to the heart.

Deoxygenated blood is received in the right atrium. From the right artery, deoxygenated blood is pumped to the right ventricle and further on to the lungs for oxygen uptake. From the lungs, oxygenated blood is being returned to the left atrium of the heart via pulmonary vein. The left ventricle pumps oxygenated blood further on to be distributed to different organs. [17, p. 320–321]; [27, p. 451–452]

2.4 The autonomic nervous system

Autonomic nervous system (ANS) is a part of the peripheral nervous system. ANS is functioning unconsciously and it controls internal body functions such as heart rate (HR) and respiratory rate. ANS is also responsible for reactions like fight or flight. The core task of ANS is to keep the invasive conditions stable; in other words, maintain homeostasis. The autonomic nervous system can be defined as nervous systems that link the efferent pathways from the brain to the specific inner organs. The autonomic nervous system is the link between the heart and the brain for instance. [27, p. 333-334]

The autonomic nervous system can be divided into two subsystems, which are sympathetic nervous system (SNS) and parasympathetic nervous system (PNS). In a nutshell, those two subsections can be described with the following: the sympathetic nervous system is responsible for activities like fight or flight and the parasympathetic nervous system is responsible for activities like rest and digest [18, p. 171–172]. Taking this concept to the heart, it can be said that the sympathetic nervous system increases the heart rate whereas the parasympathetic nervous system predominates at rest decreasing the heart rate [18, p. 166–168]. The PNS has nerve endings to the sino-atrial node, atrio-ventricular node and to the atrial myocardium. The SNS has nerve endings all over the myocardium. [28]

The balance between SNS and PNS is controlled by the cardiovascular center located in medulla in the brainstem. In the cardiovascular center the sensory feedback from baroreceptors (from the heart), chemoreceptors and proprioceptors are combined with the higher order input from the cerebral cortex. Based on these inputs the cardiovascular center controls the HR via shifting the relative balance between the PNS and the SNS. [6]

The pathways of the autonomic nervous system do not go straight from the relevant brain region to the effector organ. The ANS neurons pass through autonomic ganglia that are a cluster of nerve cell bodies. The autonomic ganglia are located outside the central nervous system (CNS) [18, p.165–166]. Peripheral parasympathetic and sympathetic nervous systems are based the two different populations of neurons; preganglionic and postganglionic neurons [27, p. 334–335]. Cells that connect the autonomic ganglias to their target organs are called postganglionic fibers. Preganglionic fibers connect the autonomic ganglia and the CNS. The somatas of the pregangionic fibers are usually located in the brainstem and in the spinal cord. The somatas of the somatic system are also located within the same region in the

brainstem. Therefore the autonomic and the somatic systems in brain-level are practically indistinguishable. [27, p. 333–334]

To sum up the tasks of the post and preganglionic nerves it is said that the preganglionic neurons take the impulse from the CNS to the postganglionic neuron, which passes it on to the target organ [17, p. 220].

2.4.1 Parasympathetic nervous system and the heart

Parasympathetic nervous system modulates the heart rate via the tenth cranial nerve called vagus nerve. The vagus nerve modulates HR via innervations to cardiac pacemaker nodes, the atrioventricular (AV) node and the sino-atrial (SA) node. Vagus nerve has also innervations straight to cardiac muscle [6]. The intrinsic rate of cardiac actionpotentials according to SA node is around 60–100 potentials per minute, and the rate decreases with age. Parasympathetic modulation of the heart can slow the HR down to 20–30 bpm. It predominates at rest and is able to briefly stop the heart [6].

The HR changes caused by the PNS are much faster than ones caused by the SNS. Signaling speed in the PNS nerves is faster than in the SNS nerves [27]. In addition to that, the PNS mediates the HR via acethylcholine binding which is practically instantaneous [29]. Postganglionic nerve terminals release acytolcholine that affects the permeability of nodal cells. Altered permeability causes change in potassium level in the cell, and further on, that causes hyperpolarization of the membrane potential. In other words, it takes a longer time to reach the critical potential that launches actionpotential because the membrane potential is below normal resting potential ($-70mV$). This chain of events eventually decreases HR. [18, p. 279–280] The decreasing effect of a single vagal impulse is rather short. A vagal impulse affects the ongoing cardiac cycle, depending on its phase, and only one or two following cardiac cycles. When a vagal impulse is faded away, HR returns to the previous rate. Therefore fast changes in HR are modulated by the vagus nerve. [6]. Vagal impulse does not have an effect on the cardiac force of contraction [18, p. 168].

PNS preganglionic nerve bodies are typically located in the brainstem and spinal cord (sacral segments S3–S4) [18, p. 166]. Parasympathetic ganglia (cluster of nerve cell bodies) are located close to the target organ [17, p. 219]. Short postganglionic fibers and long preganglionic fibers are typical for PNS [18, p. 166].

Cardiac vagal neurons in the brainstem are silent by their nature. This means that any signal coming from these neurons must be first generated elsewhere. Therefore the activity of these premotor cardiac vagal neurons in the brainstem is a result of different inputs, i.e. inhibitory and excitatory neurotransmission [30].

2.4.2 Sympathetic nervous system and the heart

The sympathetic nervous system has innervations to many regions of the heart, such as ventricular and atrial myocardium and pacemaker cells [31, p. 6–7]. Especially efferent nerves directing to pacemaker cells, AV and SA nodes are the key pathways when modulating the HR. Typically this modulation accelerates HR. On the contrary to the effects of PSN, in the nerve terminals of SNS, epinephrine (E) and

norepinephrine are released. These neurotransmitters bind to beta-adrenergic ($\beta 1$) receptors. This process accelerates the depolarization in SA and AV nodes, and eventually HR increases. [6]. The SNS impulse does not only accelerate HR, but it also increases the cardiac contraction force, unlike its counterpart PNS [27, p. 336]. Without any input from the SNS, the heart will beat with the intrinsic rate of the pacemaker cells [6]. For example, high heart rates in an exercise are of sympathetic origin.

The sympathetic system is relatively slow and it may take even five seconds before the SNS stimulation has an effect on HR. Likewise, the SNS impulse does decay slower. A brief stimulus from the SNS can affect the HR for 5–10 seconds. [6] For a longer stimulus it may take 20–30 seconds to reach the maximal response. This is not due to slower neuronal discharges, but rather it is an issue of slowly responding heart. [31, p. 7]

2.5 Heart rate variability

"A healthy heart is not a metronome" [6]. A healthy heart does not beat in a metronome accuracy, but there are variations in time intervals between the beats (Fig.5). The variation of time intervals between the beats is called heart rate variation (HRV) [6]. Analyzing HRV is a relatively easy method to explore the ANS. The heart rate is modulated mainly by changes in the ANS activity and therefore HRV is considered as a marker of the ANS activity [28]. Respiratory control system and blood pressure (BP) also give their input to the variations of the heart rate. Together those interactions produce short term rhythms in HRV [6].

HRV can be measured using techniques like electrocardiogram (ECG) or photoplethysmograph (PPG) [6]. In this study, all the HRV measurements are extracted from ECG signals. In order to extract HRV data, it is essential to detect R spikes from QRS complex (see figure 4 for QRS complex). The series of time intervals between adjacent R peaks form a vector that is called RRi data. The RRi data is the core input for any HRV calculation. The most common analysis of the RRi is usually done in time domain, using both linear and non-linear statistical methods [6]. The RRi can also be analyzed in frequency and time-frequency domains [28].

RRi data is typically presented in a plot called tachogram [31, p. 179]. In the tachogram, the time between adjacent R peaks (RRi) is presented as a function of time (cumulative measurement time). For tachogram see figure 6. The heart rate is usually presented in beats per minute (Bpm) that be calculated from RRi with equation 1 [27, p. 452].

$$\mathrm{HR} = \frac{60}{\frac{\mathrm{RRi}}{1000}} \tag{1}$$

Where the HR is heart rate expressed as beats per minute and the RRi is the time between adjacent R peaks in millisecond.

The HRV concept is clarified in figure 7. The term HRV is a higher level term that is used to refer to the phenomena of variation in heart rate intervals. It also covers a wide variety of different calculation formulas for different variables. In order

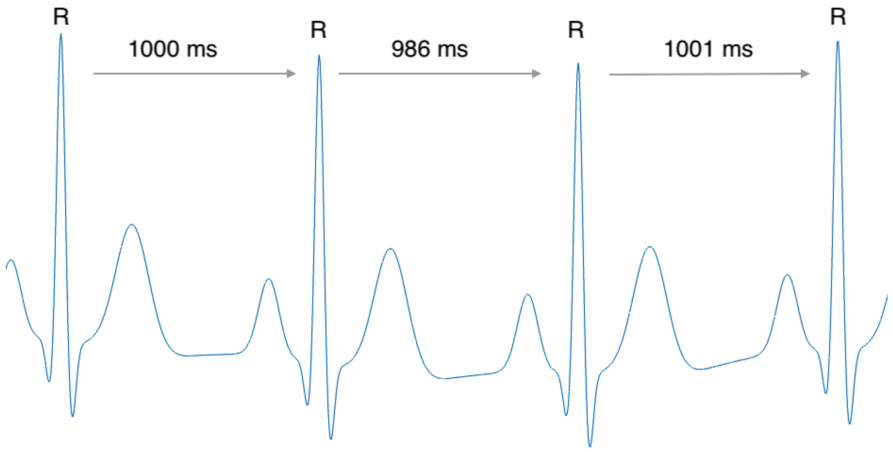

Figure 5: ECG recording with clear R peaks. Numbers present the time between adjacent R peaks in milliseconds (RRi).

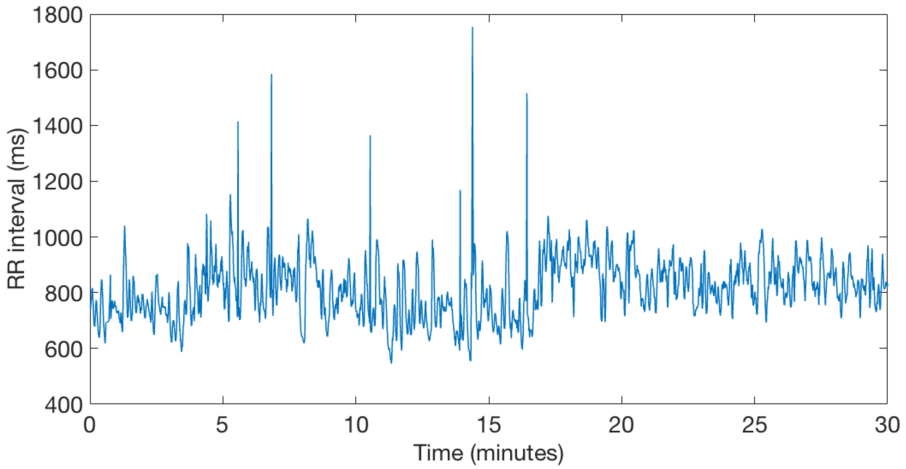

Figure 6: An example tachograph representing RRi data

to get a grasp of this phenomena, a technique to measure heart rate is needed. In order to calculate HRV variables, such as root mean square of successive difference of RRi (RMSSD), one must have beat-to-beat intervals data extracted from the ECG measurement for example.

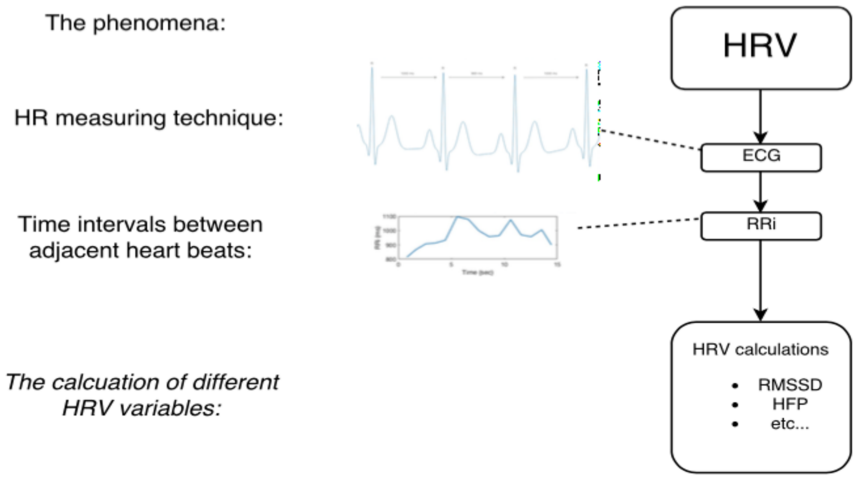

Figure 7: The concept of heart rate variability. HRV is an umbrella term that covers different HRV variables. In between, there are two compulsory phases: measuring the heart rate and extracting beat-to-beat time intervals from the measured heart rate.

2.5.1 HRV and respiration

The synchrony of respiration and heart rate variability is a physical phenomenon. It was first discovered more than 80 years ago by Adrian et al. (1932). Nowadays this synchronization is called respiratory sinus arrhythmia (RSA). In practice, RSA is a phenomenon where heart rate decreases during exhale and increases during inhale. [32]

RSA is strongest in infants and it is attenuated along with ageing [32]. RSA can be diminished by multiple diseases effecting cardiopulmonary actions such as coronary artery disease. Personal fitness also affects the magnitude of RSA and it is stronger among athletes [32]. Therefore RSA can be considered as a marker of "cardiac age" [32]. The existences of RSA seems to be much more than just a by–product of reflexes. RSA is a biological phenomenon, and it may enhance pulmonary gas exchange for instance [32].

Respiration is modulated by the autonomic nervous system. Respiration can hence be used for observing the status and activity of the ANS. [33] Cardiac parasympathetic vagal activity is also under the influence of respiration. The activity of these cardiac vagal neurons is an output of excitatory and inhibitory neurotransmission in the brainstem. Respiration seems to have an effect on this balance [30]. During insipiration, clycinergic and gamma-aminobutyric acidnergid (GABA) neurotransmission inhibits cardiac vagal neurons in the brainstem and the HR increases [30]. On the contrary, during expiration the HR decreases. An example of the effect of RSA on an RRi tachogram is presented in figure 8.

The respiratory rate is typically within HF frequency band (0.15–0.4 Hz) during rest. The lower limit of 0.15 Hz is corresponding to 9 breaths per minute and

the higher limit of the HF band 0.4 Hz is corresponding to 24 breaths per minute. Respiratory rate can be detected relatively accurately from the RRi data as long as it stays within the frequency range of the HF band [33]. A simple, but rather accurate approximation of respiratory rate is to use the peak frequency in the power spectral density curve of the HF band (HF peak). Respiratory rate is known to follow HF peak rather accurately [31, p. 111-112].

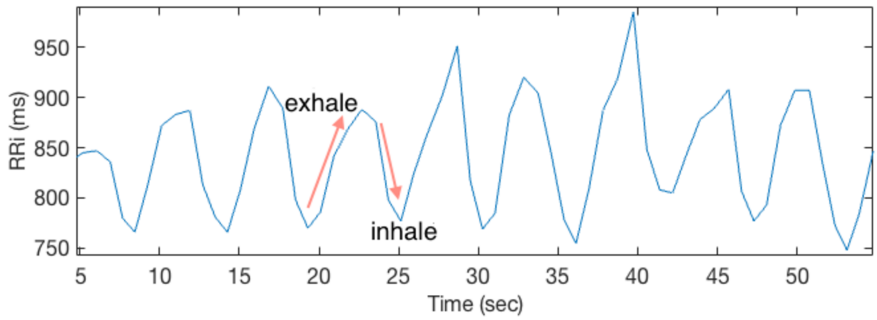

Figure 8: RRi tachogram with RSA

2.5.2 The composition of beat-to-beat interval signal

Beat to beat interval signal (here RRi) is usually divided into four different segments based on frequency bands. Those bands are high-frequency band (HF) 0.15–0.4 Hz, low-frequency band(LF) 0.04–0.15 Hz, Very-low-frequency band (VLF) 0.0033–0.04 Hz and ultra-low-frequency band (ULF) 0–0.003 Hz [9]. In this study, LF and HF bands are used.

The activity in HF band represents parasympathetic activity due to fast effects of parasympathetic stimulus on HR. The effects of respiration to HR are prominent on HF band [34]. The phenomena where heart rate changes as a function of respiration, is called respiratory sinus arrhythmia (RSA) [6]. Cardiovascular center in medulla inhibits vagal stimulus during inhalation, RRi decreases and HR increases. During exhalation vagal stimulus is stronger and RRi increases (HR decreases) [6].

The activity in LF (0.04–0.15 Hz) band is thought to represent mainly sympathetic activity. Nevertheless, it still includes a vagal component. The presence of vagal component was proved by comparing the spectral power in LF band (LFP) before and after total vagal blockade. LFP was reduced after blocking vagal stimulus [6]. The LF band is also called the *baroreceptor range* [6] due to the fact that it reflects baroreceptor activity during rest [6, 29]. SNS is able to produce activity with an approximate maximum of 0.1 Hz, therefore activity above that is a parasympathetic origin. When respiration rate decreases to below nine breaths per minute the effects of respiration to RRi are seen in the LF band. [6]

2.5.3 HRV during sleep

Nightly HRV varies in a sleep-stage specific manner during sleep [35]: In a study done among healthy males, the HR was found to decrease in sleep stage 1,2,3 and 4. Along with decreased HR, an increase in RSA was detected. Whereas in REM sleep, an increment in HR and decrement of RSA was found. During REM sleep HR was found to be even higher than during wake. Frequency peak in HF band was detected to be greater in slow-wave sleep. This peak represents respiration frequency. Falling asleep (from wake to NREM sleep) was detected to decrease LFP and increase HFP. In REM sleep HFP decreased to the same level as during wakefulness. [35] Heart rate is detected to either decrease or increase with ageing. Vagal activity was found to decrease with ageing and therefore the variation in beat to beat intervals tends to decrease also. [36]

To summarize the nightly HRV studies, it may be concluded that both HR and HRV increase during REM sleep. During NREM sleep both of these tend to decrease [29]. During sleep, HRV is higher and sympathovagal balance turns towards the predominance of parasympathetic nervous system (PNS) and the effect of SNS decreases. [19, 29]. More detailed summary of sleep stage specific changes are presented in table 2.

HRV in slow-wave sleep

Traditionally sleep and sleep phases are studied with a technique called polysomnography. This setup is however rather expensive [37], and hard to use in home environment. Nowadays it is possible to extract different stages of sleep even from the RRi data [38].

Slow-wave sleep (SWS) is an optimal condition for measuring the current status of the autonomic nervous system. During SWS the vagal modulation of the heart predominates and therefore the HFP is relatively high [38]. The ratio of the LFP and the HFP (sympathovagal balance) decreases due to high HFP values [37, 39]. SWS is also visible in nonlinear HRV analysis. Short-term variations in the HR are typically stronger in SWS than in REM sleep for example [38] (fig.9). This can be seen from the distribution in a return map (Poincare plot) where the data is plotted against itself with one sample offset (RR(n) on the x axis and RR(n+1) in the y axis). During the SWS the cluster in Poincare plot is round shaped (figure 9 A) [40] and the interbeat autocorrelation coefficient (rRR) is typically low [38].

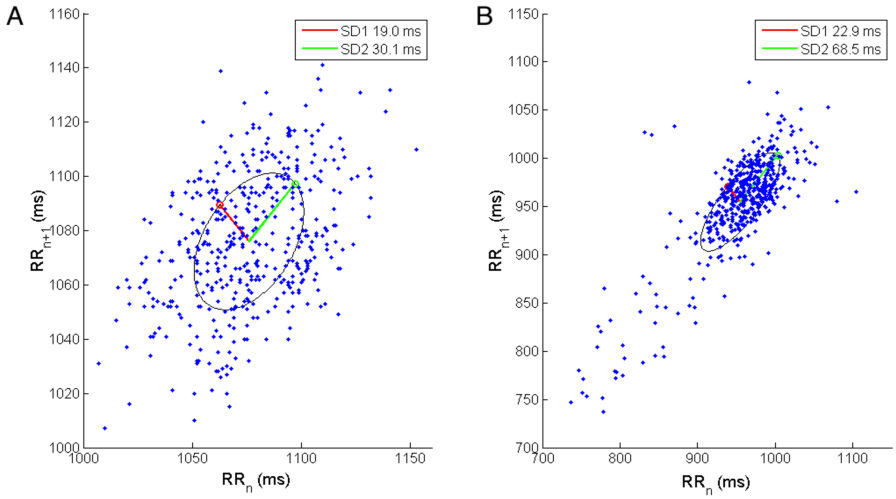

Figure 9: Poincare plots, SWS at left and non-SWS at right.

Table 2: HRV during sleep [29, 35, 36, 38, 39, 41–43].

Sleep stage	**HRV**	**Other**
Sleep onset	Increased RRi. Decreased HRV. Respiration stabilizes. LF/HF ratio decreases	VLF decreases just before sleep onset
REM	Decreased HRV. RSA decreased. High HR	Sympathetic activity and parasympathetic withdrawal. RRi can be lower than when awake.
S1	RSA increases	PNS predominance, which decreases with ageing. Breathing becomes deeper and more regular when entering N-REM sleep.
S2	RSA increases	PNS predominance, which decreases with ageing.
S3	RSA increases	PNS predominance, which decreases with ageing.
S4	Decrease in LF/HF ratio due to high HF power. RSA is at its strongest	PNS predominance. RRi highest. Describes sympathovagal balance rather well [39].

2.5.4 Physical exercise and HRV

Physical exercise affects internal functions of a body. This internal balance is maintained by the autonomic nervous system. The effects of training can be seen by observing how autonomic nervous system modulates the heart. For example, heavy training disturbs homeostasis by turning autonomic balance to sympathetic predominance [44–47].

In a study done among middle-distance runners, a significant increase in nocturnal HR between the first and third week of the overload phase was detected. In the same study, nocturnal HR decreased significantly between the last week of overload phase and the recovery week. [44]

In HRV analysis the researchers were able to found up to 40% decrease in nocturnal HFP with a significant rebound during the recovery phase. The nocturnal HRV parameters were calculated from a time windows of four hours. The window was chosen from midnight to 04:00 Am. It was concluded that heavy training shifts the nocturnal cardiac autonomic balance towards sympathetic predominance [44].

Athletes with diagnosed overtraining did not have disturber cardiac autonomic modulation during nocturnal sleep. The disturbance of the autonomic was present in a supine phase of the orthostatic test performed at mornings. LFP was lower in the overtrained group than in the control group. [45]

In an other study with international-level cross-country skiers, an increased in nocturnal HR between heavy and light training days was found [46]. No significant difference in HRV was detected. In the end of the overload phase, there was a significant decrease in nocturnal LFP and HFP along with increased HR, compared to the recovered state before overload training. [46].

In a very recent study, nocturnal HRV between high intensity training group and the control group performing aerobic training with constant load was compared [48]. The authors detected an increase in nocturnal HFP in the high intensity group. No significant differences in control group was detected. It was concluded than cumulative training load in high intensity group was not high enough to accumulate fatigue and shift sympathovagal balance towards enhanced sympathetic tone. A static time window of four hours was used for nocturnal HRV calculations. The window was chosen to begin 30 minutes after going to bed. [48]

Bucheit et al. (2004) investigated the effects of physical exercise on nocturnal HRV in a different way. The fact that Bucheit et al. (2004) used a polygraphic sleep recording to assess the desired SWS phase from the RRi recording, sets this study apart from previously mentioned studies. The authors used a stationary 5 min segment from the first SWS phase that lasted more than 15 minutes [39]. A significant increase was found in HFP and RMSSD during SWS the night after moderate training. The night after heavy training did not differ from control group with a sedentary day. [39]

To summarize these findings, it can be concluded the nocturnal functions of the ANS seem to be rather stable. The cardiac vagal activity measured by HRV can increase after moderate intensity training. With extremely heavy training the HRV parameters of cardiac vagal activity can either increase or decrease.

3 Research materials and methods

The goal of this study was to explore the possibilities of detecting fatigue from nocturnal RRi measurement.

The analysis performed in this study can be divided into two phases. In the first phase, the difference of mean values was tested. This was done on a group level. For example, a test was performed whether the difference between the nocturnal mean RRi is significantly different from the mean RRi in the orthostatic test (section 4.1). In the second phase, a correlation analysis between all the nocturnal HRV variables and the orthostatic tests was performed (section 4.2). The purpose of this was to find out which of the variables behave the most like the HRV variables in the orthostatic test.

A previously collected dataset was used in this study. The data were collected from a training intervention study. It consisted of nocturnal RRi measurements, orthostatic tests and heart rate readings from exercise sessions. The nocturnal measurements and the orthostatic tests were done approximately every third day for eight weeks. There were eleven participants in the data set (n=11). All the participants were club level runners. The participants were aged on average 30 ± 2 years. All the participants were nonsmokers and none were obese ($BMI <= 24 \frac{kg}{m^2}$). The participants were in good physical condition ($V0_2max = 57 \pm 6 \frac{ml}{kg*min}$).

The data collection lasted for eight weeks, during which the participants followed a progressive training program. The program included from four to six heart rate guided training sessions weekly. In HR guided training sessions, the participants followed their HR with Polar RS 800CX heart rate monitor (Polar Electro Oy, Finland, Kempele). They were instructed to keep their HR within the predefined HR zones during the exercise. The exercises were designed to be moderate (80-90 % of HR at ventilatory threshold (VT)) or high-intensity level (>90 % of HR at VT).

The measurement system for the nocturnal RRi and the orthostatic tests consisted of Polar RS 800CX heart rate monitor, Polar chest strap and Polar Wearlink W.I.N.D HR transmitter that was paired to the RS 800CX heart rate monitor (Polar Electro Oy, Finland, Kempele). The protocol of the orthostatic test consisted of sitting for 2.5 min followed by standing for another 2.5 min. The test was performed right after waking. The total number of analyzed night recordings was 234. The data included an equal amount of the orthostatic tests.

3.1 Data analysis

All the RRi data was managed with Matlab R2013b software (The MathWorks Inc., Natick, Massachusetts, United States). The same software was used for calculating HRV variables.

Measurement variables

The measurement variables and their formulas will be explained in this section. At first, the variables will be presented and later on in this section, a more detailed use

of the variables will be explained.

Root mean square of successive difference in RRi (RMSSD) represents short term changes in HRV and should represent parasympathetic activity [9]. RMSSD is a well established HRV variable. It is also a very popular output of commercial HRV measurements. Companies like Polar Electro Oy and Elite HRV use RMSSD as one of the main HRV variables in their products [49], [50]. The formula of the RMSSD is presented in equation 2 [9].

$$\mathrm{RMSSD} = \sqrt{\frac{1}{\mathrm{N}-1}\sum_{\mathrm{j}=1}^{\mathrm{N}-1}(\mathrm{RR_{j+1}} - \mathrm{RR_j})^2} \tag{2}$$

In the equation the N is the number of RRi:s and RR_j is the j:th RRi.

Interbeat autocorrelation coefficient is a marker of dynamic heart rate variability and sympathovagal balance [51]. Interbeat autocorrelation coefficient (rRR) was calculated as Pearson's correlation coefficient between RR_j and RR_N. Pearson's product moment correlation coefficient r was calculated with the equation 3 [52].

$$\mathrm{r} = \frac{(\sum_{\mathrm{j}=1}^{\mathrm{N}}(\mathrm{RR_j} - \overline{\mathrm{RR}})(\mathrm{RR_{j+1}} - \overline{\mathrm{RR}})))}{\sqrt{\sum_{\mathrm{j}=1}^{\mathrm{N}}(\mathrm{RR_j} - \overline{\mathrm{RR}})^2} * \sqrt{\sum_{\mathrm{j}=1}^{\mathrm{N}}(\mathrm{RR_{j+1}} - \overline{\mathrm{RR}})^2}} \tag{3}$$

The N is the number of RRi:s, RR_j is the j:th RRi and $\overline{RR}$ is the sample mean ($\frac{1}{N}\sum_{j=1}^{N} RR_j$).

The relative proportion of successive RRi with more than 50 ms difference (pNN50) represents short-term variations in RR intervals. The letters NN stands for normal-to-normal interval. NN interval is defined as the time between adjacent normal R peaks in QRS complex. The R peak is counted as normal when it is generated by sinus node depolarization. The pNN50 was calculated with equation 4 and it is presented as a percentage. [9]

$$\mathrm{pNN50} = \frac{\mathrm{NN50}}{\mathrm{NN}} \tag{4}$$

The $NN50$ is the number of the NN intervals with at least 50 ms difference and NN is the total number of the NN intervals.

A novel HRV variable *fIndex* was derived from RRi and HF peak. It was hypothesised that fIndex would represent parasympathetic activity, with a sympathetic component. In the results sections, the fIndex was compared to the orthostatic test. The fIndex was calculated with the equation 5.

$$\mathrm{fIndex} = \frac{\mathrm{RRi}}{60 * \mathrm{HFpeak}} \tag{5}$$

The RRi is the time between adjacent heart beats in milliseconds (ms) and $HFpeak$ is the peak frequency in HF band. This represents respiration.

In order to calculate frequency domain variables, the RRi data was resampled at the rate of 4 Hz, by using cubic spline interpolation. For the chosen segment of

the data, a time window of 5 minutes was applied. In frequency domain calculations a cosine-tapered (Tukey) window was applied before converting the data to the frequency domain. Conversion to frequency domain was done with a Fast Fourier transform. The high frequency powers (HFP, 0.15–0.4 Hz) and the low frequency powers (LFP, 0.04–0.15 Hz) were calculated as trapezoidal integrals of the power spectrum curve. The ration of LFP and HFP was simply calculated by dividing the LFP with the HFP. The peak frequency of the HF band (HF peak) was chosen as the frequency with the most power in the power spectrum curve (0.15–0.4 Hz).

Two novel variables were calculated from the orthostatic test, time to lowest (TTL) and HR speed (HRs).The HRs is defined as the speed of the HR changes when standing up (eq. 6–7 and fig. 10). The HRs is thought to indicate the activity of the PNS, i.e. high HRs would indicate high PNS activity. TTL is defined as the time that is required to reach the minimum RRi after standing up in an orthostatic test (equation 8 and figure 10). TTL is thought to reflect the activity of the SNS. These novel variables are also explained in figure 10.

$$\Delta\text{HR} = \frac{60}{\frac{\text{RRi}_1}{1000}} - \frac{60}{\frac{\text{RRi}_0}{1000}} \tag{6}$$

$$\text{HRs} = \frac{\Delta\text{HR}}{\text{TTL}} \tag{7}$$

$$\text{TTL} = \text{t}_{\text{end}} - \text{t}_{\text{start}} \tag{8}$$

In the equations the ΔHR is the change in heart rate during transition phases, RRi_1 is the RRi in milliseconds (ms) at the end of the transition phase, RRi_0 is the RRi in milliseconds (ms) in the beginning of the transition phase, TTL is the time to the lowest RRi value during transition phase in seconds, t_{end} is the time at the end of the transition phase in seconds and t_{start} is the time in the beginning of the transition phase in seconds.

Orthostatic tests

The participants performed an orthostatic test at mornings, as soon as possible after waking up. The test consist of three phases: sitting, transition and standing phases. The test was started in a sitting position. After 2.5 min the participant stood up. Standing up is called the transition phase. Finally, the participant stands for another 2.5 min. The outcome of the test is a 5 min long RRi recording from which the HRV variables can be calculated. A sample of an orthostatic test RRi recording is presented in figure 10. In the figure sitting phase, transition phase and standing phase are pointed out.

The data from the orthostatic tests were analyzed in the time domain. The variables calculated from the orthostatic tests were: root mean square of successive difference of the RRi (RMSSD), mean RRi,the relative proportion of successive RRi with more than 50 ms difference (pNN50) and two novel variables, time to lowest (TTL) and HR speed (HRs). RMSSD, mean RRi and pNN50 were calculated separately for sitting and standing phases. TTL and HRs were calculated only from

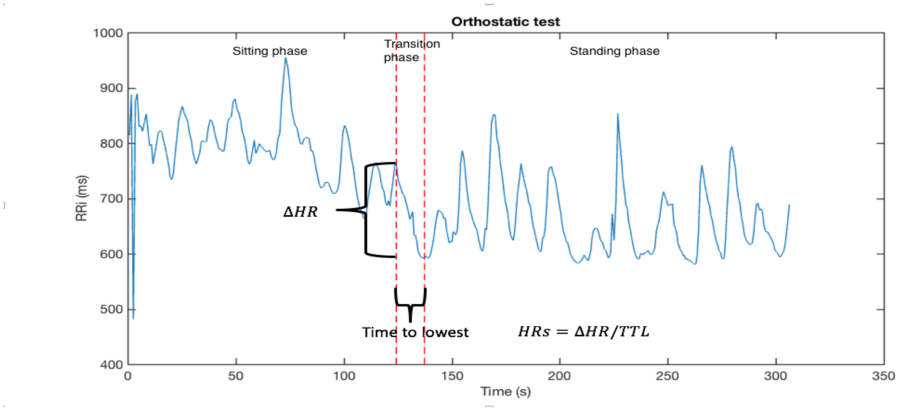

Figure 10: RRi recording of an orthostatic test. The equation of HRs is embedded in the figure.

the transition phase. These novel variables are clarified in figure 10 and defined in equations 6,8 and 7.

RMSSD and pNN50 were calculated separately for sitting and standing phases (eq.2, 4). RRi is expressed as a mean value of the phase. The calculation window of HRV variables was adjusted for sitting and standing phases individually for every test. This was done due to the variation in the test lengths.

The series of orthostatic test results were then averaged over three measurement points (i.e. one number per test variable per day, averaged over three days). Averaging was done separately for every participant. The variables calculated from the orthostatic test are summarized in table 3.

Table 3: HRV variables calculated from the orthostatic test

Variable	**Test phase**	**Unit**
RMSSD	separately from sitting and standing phases	ms (millisecond)
pNN50	separately from sitting and standing phases	percentage (%)
TTL	transition phase	sec
HRs	transition phase	$\frac{bpm}{sec}$
mean RRi	separately from sitting and standing phases	ms

Nocturnal RRi data

Sleep data were analysed using two different data segments. The first segment was chosen to last for two hours. It began 30 minutes after the beginning of the data. Later on this segment will be referred as *Evening segment*. It should consist of approximately one to two sleep cycles.

The idea behind the second segment was to focus on a certain sleep phase. The goal was to find an artifact free segment, that would characterize slow–wave sleep. This segment will be called *SWS segment*. Each SWS segment was selected manually and chosen to be five minutes long. The selection criteria for SWS segment was adapted from earlier studies [37, 38, 43]. For more detailed info on HRV during slow wave sleep, see chapter 2.5.2. The criteria for choosing the segment was the following:

- Low $\frac{LFP}{HFP}$ ratio, typically close to 1 or below
- High RRi, compared the level of night recording
- Relatively low interbeat autocorrelation coefficient (rRR), typically below or close to the mean rRR of the data

No absolute values for the selection criteria were defined. The data consisted of high interindividual differences and therefore absolute value limits for the selection criteria were not suitable for this study. The chosen segment was further verified with Poincare analysis. If the distribution was round shaped (figure 9 A), the segment was approved as an SWS segment. The chosen segment was visually inspected to be free of flagrant recording artifact. The first 30 minutes of the recordings were excluded from the segment selection, to ensure that the participants were asleep. An example of the SWS segment is provided in figure 11.

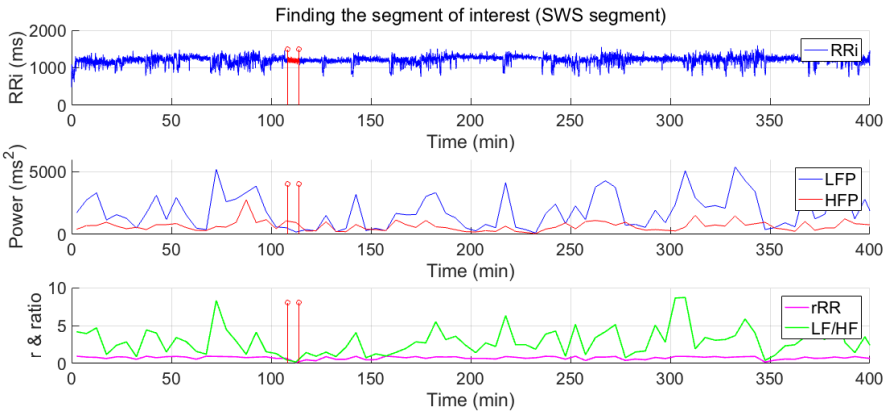

Figure 11: A sample SWS segment. The selected SWS segment is between the red marker lines.

HRV analysis from the nocturnal RRi

Time domain and frequency domain analysis were performed to both segments. In time domain RMSSD, rRR and pNN50 were calculated (eq. 2–5). In the frequency domain, HFP, LFP, HF peak and $\frac{LFP}{HFP}$ ratio were calculated.

For the evening segment, the HRV variables were calculated using a window of 5 minutes. The evening segment consisted of 24 of those 5 minutes windows. No overlap was used between the windows. The results of evening segment calculations

are expressed as mean values of all the 5 minutes windows (i.e. one value per night which is the mean of the 5 min window values). The results of the calculations from both segments were averaged over three measurement points (i.e. one value per night averaged over three nights). This was done with a moving average filter.

Statistical analysis

In the first phase of the analysis, Wilcoxson rank sum test was used to study group differences between nocturnal data segments (SWS and Evening segment) and orthostatic test conditions (sitting and standing). The familywise error was corrected with a Bonferroni correction from the results that are presented in section 4.1. After applying the Bonferroni correction, the statistical significance was approved when $p < 0.0083$.

In the second phase of the analysis, the data were first tested for normality with Kolmogorov-Smirnov test. The data did not meet the assumptions behind parametric tests, and therefore non-parametric test was used. Kendall's rank correlation (Kendall's τ) was used to evaluate relationships between the variables. Kendall's tau was chosen due to its suitability for relatively small sample sizes [53]. The key analysis of this study was the correlation analysis between the nocturnal HRV variables and the variables calculated from the orthostatic tests. The correlation was calculated between all the nocturnal variables and all the variables calculated from the orthostatic test. The correlation was approved to be significant when $p < 0.05$. The familywize error was not corrected in the comparison of the nocturnal HRV variables and the orthostatic test variables. The risk of false positive does therefore exist.

The statistical analyses were done with Matlab R2016b (The MathWorks Inc., Natick, Massachusetts, Unites States) and RStudio 1.0.143 (RStudio, Boston, MA, Unites States).

3.2 Descriptive data

Section 3.2 describes the data. It is meant to give the reader an overview of the data used in this study. The following sections 4.1–4.2 present the results of group level comparisons and the correlation analysis between nocturnal parameters and orthostatic parameters

On average there were 21 nocturnal recordings per participant and the average recording length was 8.3 hours. The descriptive values from the nocturnal measurements are presented in table 4.

Table 4: Descriptive data of the night measurements

N	Nights per Id	Mean night length (hours)	Mean HR (bpm)	Mean HR (bpm, SWS)
11	21 ± 3	8.30 ± 0.3	57 ± 2	52 ± 2

Note: HR = heart rate; bpm = beats per minute; SWS = SWS segment;

Values expressed as mean $\pm std$

Descriptive figures

In the following section, some remarks and comments about the data will be presented. The data from the orthostatic test and both nocturnal conditions are presented in figures 12–15. The main remarks of these figures will be explained. The figures consist of bars that are to interpreted as a mean value of a certain variable over the entire study. The red whiskers on each bar represent the 25th and the 75th percentile of the variable. The results of regression analysis between orthostatic tests and nocturnal conditions are covered in section 4

Figure 12 summarizes the variables calculated from the orthostatic tests. Even if the participants in this study were a rather homogenous group, there are large interindividual differences. For example, RMSSD of participants 1–7 is considerably lower that RMSSD for participants 8–11 (figure 12, top left).

The novel variable of HRs (figure 12 bottom right), seems to behave almost in a similar manner as RMSSD for instance. This was as expected since both of these variables were thought to reflect the activity of the PNS. The benefit of HRs over RMSSD is that it holds the information of the level of the RRi. This can be seen by comparing bottom left graph and bottom right graphs in figure 12. Even a short visual inspection reveals the trend, that those participants who had higher mean RRi during sitting phase received also higher HRs value.

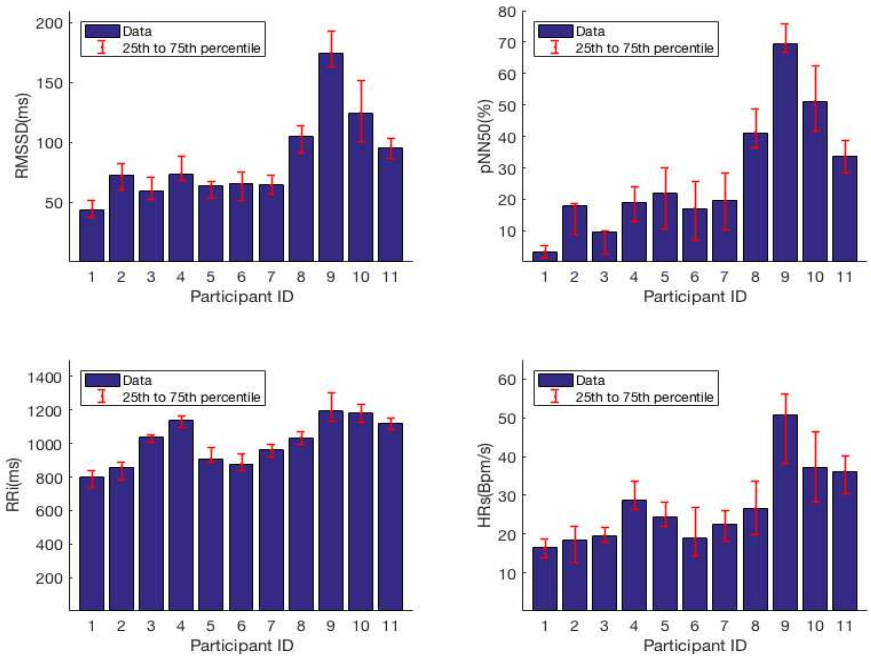

Figure 12: Variables from orthostatic tests from the sitting phase and HRs from the transition phase. Blue bars represent mean values of the variable per participant. Red whiskers represent the 25th to 75th percentile of the variable.

Figure 13 summarizes the variables from orthostatic tests. The novel variables TTL (bottom right in figure 13) seems to peak in participants two and three. These participants also had very low mean RRi (high HR) during standing phase. This is was as expected. When a person is fatigued, it should take a longer time to reach the minimum RRi after standing up in the orthostatic test. It must be pointed out that none of the participants was diagnosed with overtraining.

Figure 14 summarizes the time domain variables from SWS segment and Evening segment. The conclusion of the figure is that SWS variables tend to reflect the state of Evening segment variables. Meaning that on group level both segments seem to go hand in hand, but on a slightly different level. The main reason for this is that in many cases SWS segment is practically a subset of the corresponding Evening segment. As well as in the orthostatic test, here the interindividual differences are also considerable. The greatest difference between the segments is found from interbeat autocorrelation (rRR, bottom right in figure 14).

Figure 15 summarizes the frequency domain variables from SWS segment and Evening segment. As seen from figure 15 (top left chart) that the peak frequency of HF is relatively similar in both SWS and Evening segments. HF peak is thought to follow respiration rate rather accurately [31, p. 111-112]. We may then assume that in this particular study, the characteristics of respiration are rather similar during SWS segment and longer Evening segment.

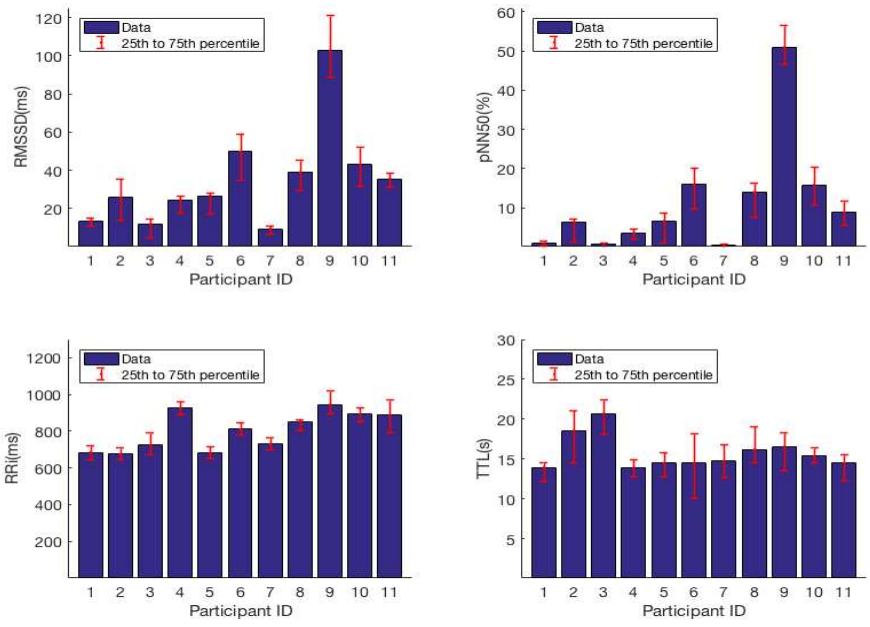

Figure 13: Variables from orthostatic tests from the standing phase and TTL from the transition phase. Blue bars represent mean values of the variable per participant. Red whiskers represent the 25th to 75th percentile of the variable. RMSSD, pNN50 and RRi values are from the standing phase, TTL calculated from transition phase.

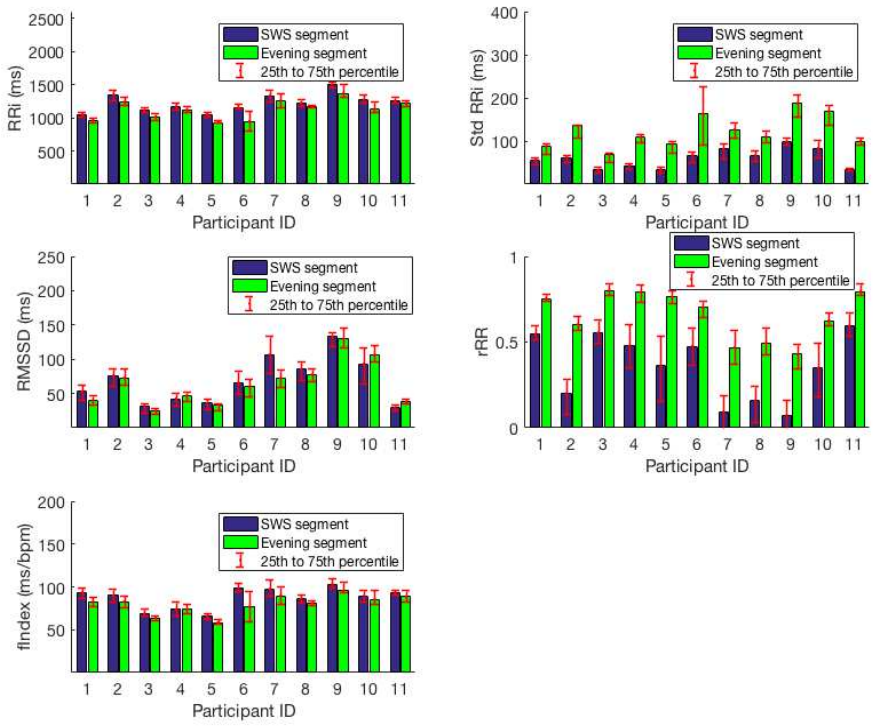

Figure 14: Nocturnal time domain variables per participant. Blue bars represent mean values of the SWS segment. Green bars represent mean values of Evening segment. Red whiskers represent the 25th to 75th percentile.

The larger difference in LF per HF ratio between SWS and Evening segment was as expected (fig. 15, top right chart). $\frac{LFP}{HFP}$ ratio was one of the selection criteria for SWS segment, and therefore the large difference was excepted. For the same reason, major differences in HF powers and LF powers occur. The high interindividual differences are to be pointed out in this figure. Participants 3–5 have very low HFP ($mean < 1000ms^2$), whereas the highest mean values reach nearly $5000ms^2$.

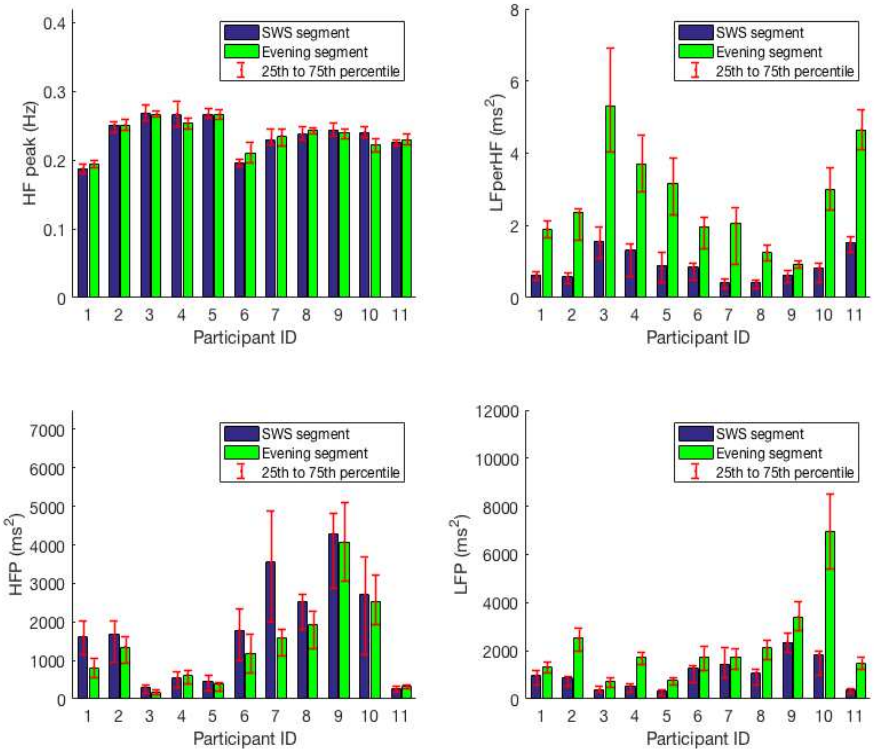

Figure 15: Nocturnal frequency domain variables per participant. Blue bars represent the SWS segment. Green bars represent the Evening segment. Red whiskers represent the 25th to 75th percentile.

4 Results and Discussion

4.1 Background results

In this section, the results of analysis between different conditions will be introduced. The purpose of this section is to highlight that the properties of the chosen conditions (SWS segment, Evening segment, sitting and standing) are different.

A paired samples Wilcoxson rank sum test was conducted to compare group means of the RRi in all four conditions. There was a significant difference in the means of the RRi in the SWS segment ($M = 1222, q(0.25) = 1107, q(0.75) = 1303$) and the RRi in the Evening segment ($M = 1121, q(0.25) = 996, q(0.75) = 1214$), ($v = 26980, p < 0.008$). The difference between sitting ($M = 1011, q(0.25) = 890, q(0.75) = 1122$) and standing ($M = 804, q(0.25) = 701, q(0.75) = 886$) conditions was also found to be significant ($v = 27005, p < 0.008$). The difference in the mean RRi between the SWS segment and both sitting and standing phases of the orthostatic test showed significance (sitting, $v = 26795, p < 0.008$; standing $v = 27028, p < 0.008$). The difference between the mean RRi from the Evening segment and sitting and standing phases showed significance as well (sitting, $v = 23128, p < 0.008$; standing, $v = 27017, p < 0.008$). The deviations of the analyzed mean RRi are presented in figure 16.

A similar Wilcoxson rank sum test was conducted on means of the RMSSD from the Evening segment, SWS segment, sitting and standing phases of the orthostatic test. There was a significant difference between the RMSSD in both nocturnal segments (SWS,$M = 68, q(0.25) = 38, q(0.75) = 89$; Evening segment, $M = 65, q(0.25) = 38, q(0.75) = 83$) and orthostatic sitting position ($M = 87, q(0.25) = 59, q(0.75) = 104$) standing position ($M = 36, q(0.25) = 18, q(0.75) = 43$). There was also a significant difference between the RMSSD from the SWS segment and the RMSSD from the Evening segment ($V = 17375, p < 0.008$). The deviations of the analyzed RMSSD are presented in figure 17.

The results of both, RMSSD and mean RRi, point out that the activity of the ANS is different during wake than what it is during sleep. Interestingly the RMSSD is highest in the sitting phase albeit the RRi is highest in the SWS segment. This could perhaps be due to the saturation phenomena (phenomena where HRV can decrease along with falling resting HR [54]).

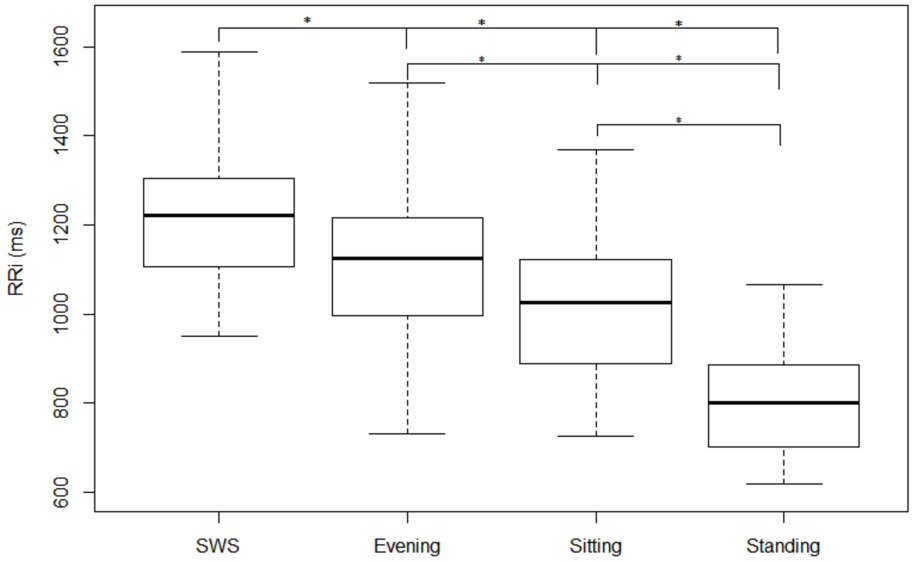

Figure 16: The deviation of the mean RRi between different conditions. $^*p < 0.008$

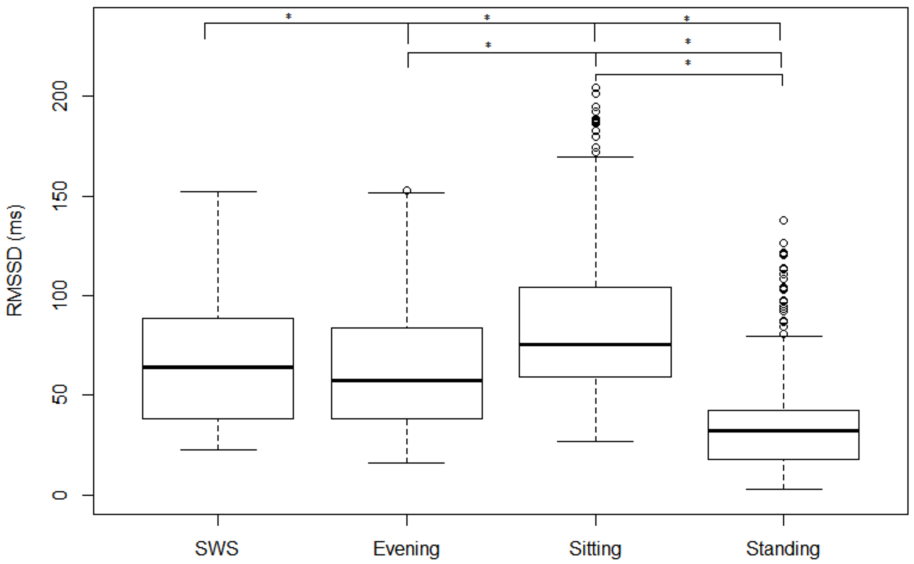

Figure 17: The deviation of the RMSSD between different conditions. $^*p < 0.008$

4.2 Individual results

In this section, the results of correlation analysis on an individual level are presented. The purpose of this analysis was to find out which of the used nocturnal HRV variables correlates the orthostatic test the most. The target of this correlation analysis was to find out whether some nocturnal HRV would behave in a similar manner than the HVR calculated from the orthostatic test. Even if correlation does not necessarily mean causality, it might be possible to replace the orthostatic test with nocturnal HRV measurement, if the correlation reaches significance. The scatter plots with the correlation of the most relevant variables are presented in figures 18–23. The more detailed numerical results of the correlation analysis are presented in tables 5–8.

Only weak correlation between sitting RMSSD and RMSSD from Evening segment ($\tau = 0.24, p > 0.05$) was observed. No statistical significance was reached on a group level (i.e. on average the correlation was not significant). Correlating the same sitting RMSSD to the RMSSD from the SWS segment resulted moderate correlation ($\tau = 0.34, p > 0.05$). On a group level, no statistical significance was reached here either. On an individual level, the number of participants with significant correlation increased. Out of 11 participants, only two reached statistical significance ($p < 0.05$) in Evening segment calculations. The corresponding number of significant correlation was doubled to four when comparing to SWS segment. There were large interindividual difference in correlations between the orthostatic sitting RMSSD and the nocturnal RMSSD.

In most of the graphs in figure 18 the measurement results resembles a mesh rather than a line or a curve. The mean correlation was $\tau = 0.26 \pm 0.17$ and there were only $\frac{3}{11}$ cases (ID1, ID4 and ID5) that reached statistically significant correlation. The differences between individual are evident. The same analysis between the sitting phase RMSSD of the orthostatic test and the nocturnal RMSSD from the Evening segment gave only a slightly different results. The correlation was lower and its standard deviation was larger ($\tau = 0.17 \pm 0.21$). The significance was reached in $\frac{3}{11}$ cases but this time the IDs were slightly different. Significant IDs were: ID4, ID5 and ID10. The deviations of the points are quite alike in both cases (fig. 18–19) and the number of statistically significant cases was the same.

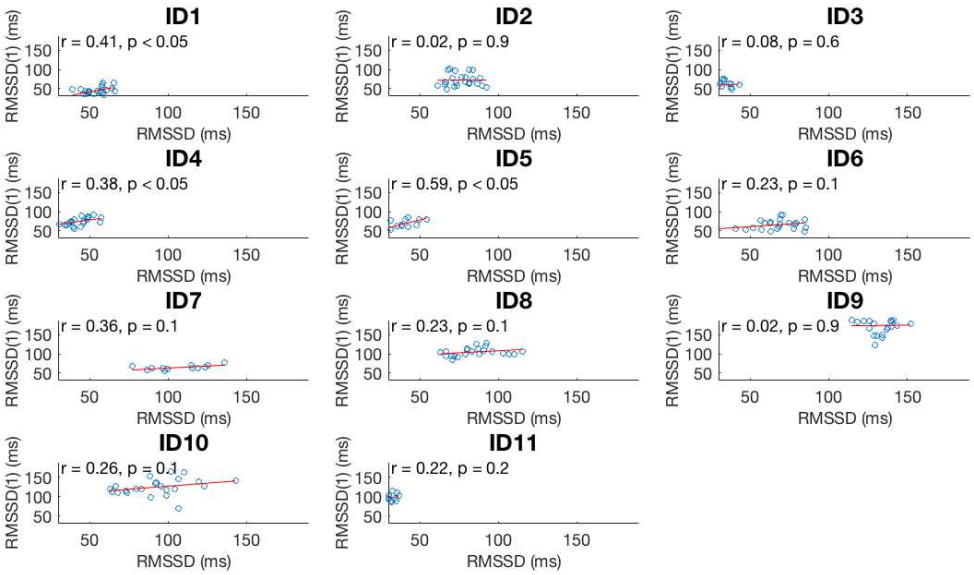

Figure 18: The correlations between the RMSSD from the SWS segment and the sitting RMSSD

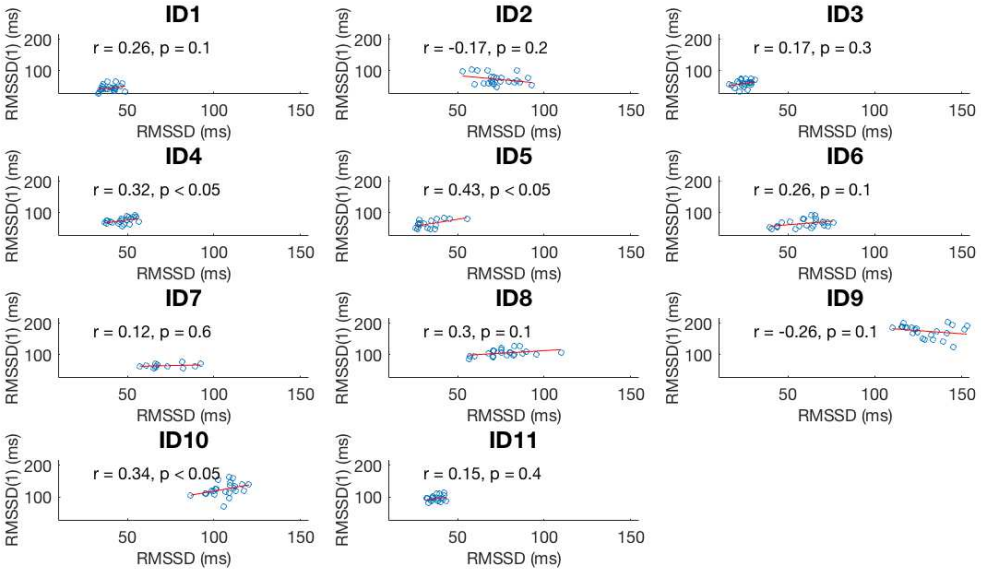

Figure 19: The correlations between the RMSSD from the Evening segment and the sitting RMSSD

The strongest correlation between orthostatic test and nocturnal parameters was found by comparing the standard deviation (std) of the RRi in SWS segment and the standing RRi of the orthostatic test. On group level this correlation was moderate, but not statistically significant (mean $\tau = -0.26 \pm 0.26, p > 0.05$). On an individual level, the correlation was significant in $\frac{8}{11}$ cases. In two cases (ID7 and ID 9) the correlation was to opposite direction than the group mean.

The correlation between the std RRi from the Evening segment and the standing RRi from the orthostatic test was not as strong ($\tau = 0.16 \pm 0.34$) and there were only $\frac{5}{11}$ cases with significance. The directions of the correlations were also not as consistent as with std RRi from the SWS segment. In $\frac{5}{11}$ cases the correlation was negative and in $\frac{6}{11}$ cases positive.

The individual correlations between the std RRi (both nocturnal segments) and the standing RRi from the orthostatic test are presented in figures 20– 21. The composition of point clouds in figure 20 is very different from previous figure 18–19. In the figure 20 the trendline (the red line plotted on graphs in the figures 18–23) seems to fit the data points much better.

To summarize the results of the correlation between std RRi and standing RRi from the orthostatic test, it can be said that the correlation is stronger and on the group level, more consistent when using the std RRi from the SWS segment. The question of possible causality of the std RRi from the SWS segment and the standing RRi from the orthostatic test remains to be answered by future studies.

The results of the correlation between the fIndex and the standing RRi from the orthostatic test are presented mainly due to the novelty of the fIndex variable. In the

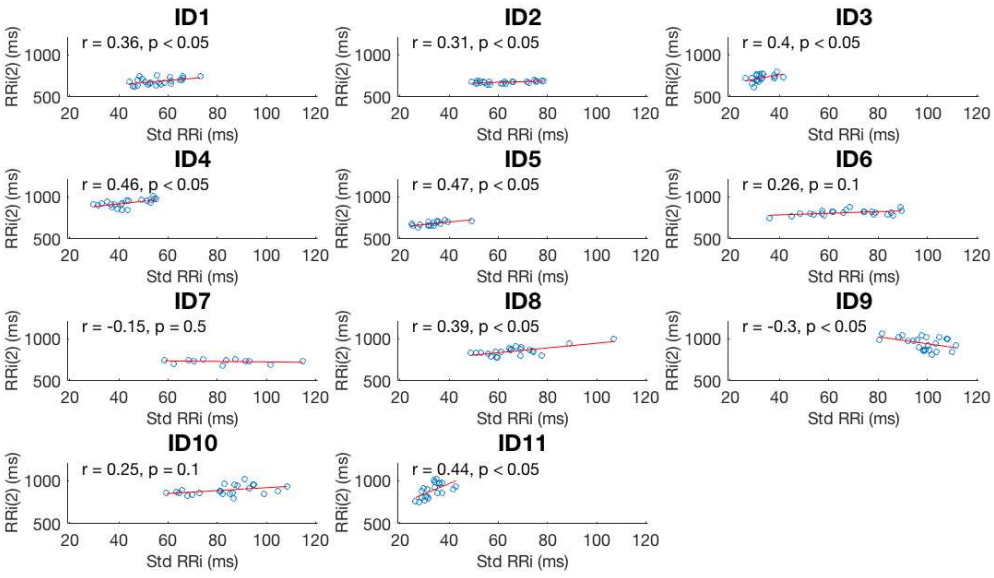

Figure 20: The correlations between the RRi in standing position and the nocturnal std RRi from the SWS segment

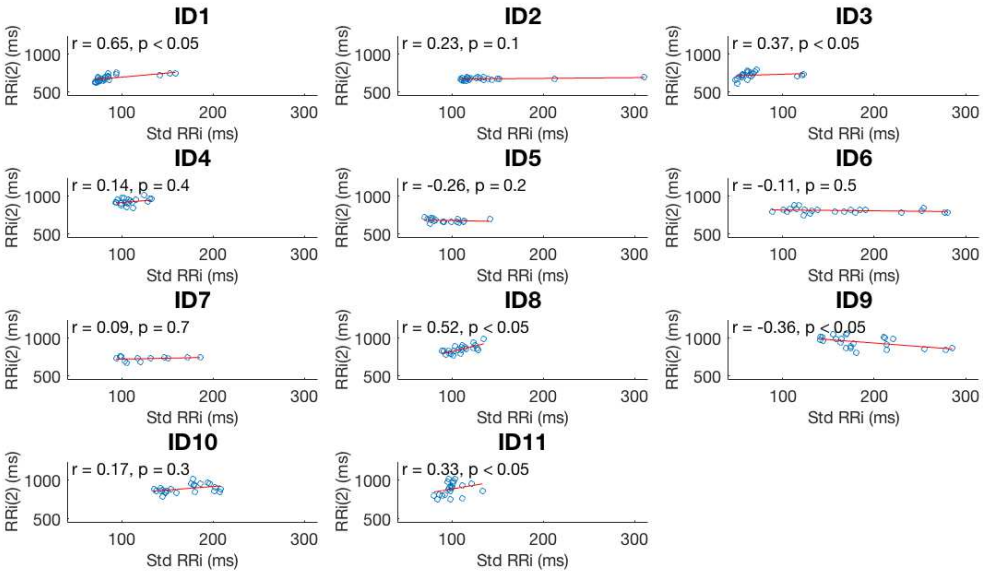

Figure 21: The correlation between the RRi in standing position and the nocturnal std RRi from the Evening segment

context of correlation analysis, the fIndex did not offer any better results than the already existing HRV variables. In the SWS segment analysis the mean correlation was close to zero ($\tau = 0.02 \pm 0.27$) and only $\frac{3}{11}$ cases were found to be significant. Even in these three significant cases, there are inconsistencies about the direction of the correlation. In one case the correlation is negative and in two cases positive.

The fIndex calculated from the Evening segment correlated slightly stronger to the standing RRi ($\tau = 0.06 \pm 0.31$). There were $\frac{4}{11}$ significant cases. The inconsistency in correlation direction between different cases was strong. Out of four significant cases in two, the correlation was positive and in two it was negative.

The individual correlations with trendlines are presented in figure 23

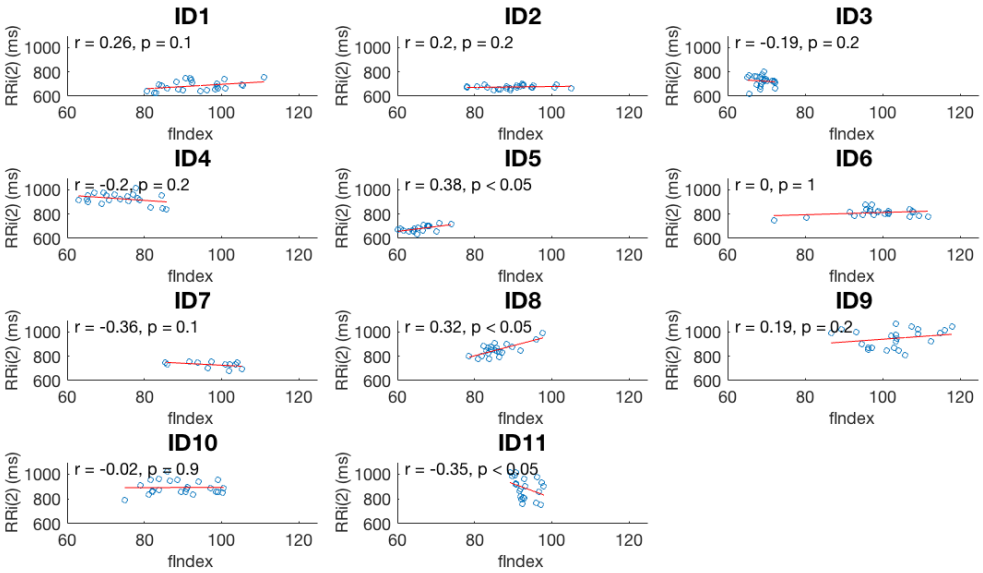

Figure 22: The correlation between the RRi in standing position and the nocturnal fIndex during the SWS segment

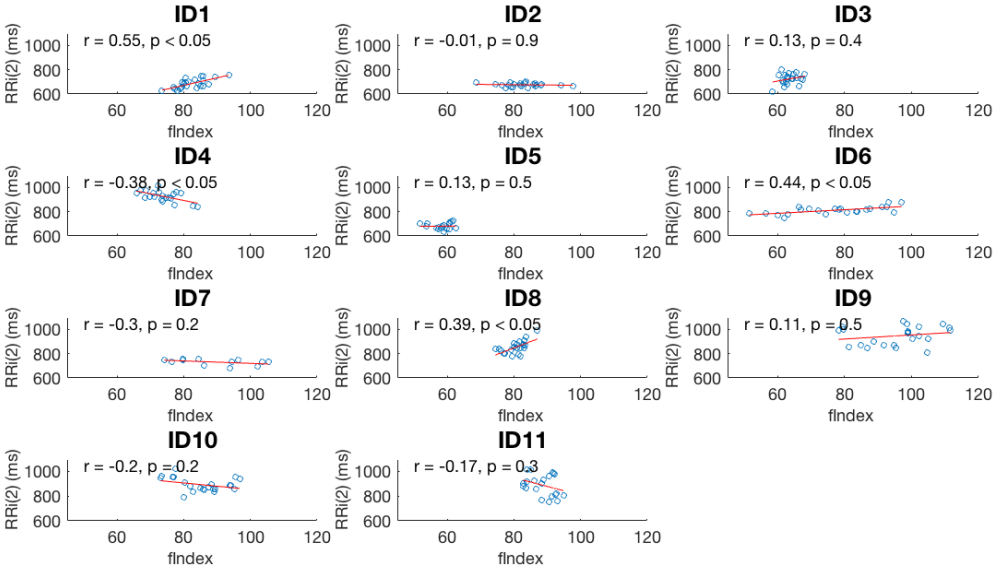

Figure 23: The correlation between the RRi in standing position and the nocturnal fIndex during the Evening segment

In addition to the previously presented results, a relatively good number of significant cases was achieved between the mean RRi from the sitting phase of the orthostatic test and the nocturnal RMSSD from the Evening segment. In that case, the number of significant cases was seven (mean $\tau = 0.18 \pm 0.30$). On average the strongest correlation was found between nocturnal RMSSD and pNN50 from sitting phase ($\tau = 0.34 \pm 0.24$). There was however only five significant cases between these variables (table 6).

The following tables (5–8) present the mean correlation coefficient of all the variables listed in section 3. All the correlation coefficients are rather low. One possible reason for this is the inconsistencies in correlation directions. Table 6 tells the number of significant cases out of 11.

The average correlations between Evening segment and orthostatic test are presented in table 7 and the numbers of significant cases are presented in table 8. In general, the correlation coefficients are lower than in previous SWS segment tables. The strongest correlation was found between the nocturnal standard deviation of RRi (Sdt RRi) and RMSSD from sitting phase ($\tau = 0.27 \pm 24$). The corresponding number of significant cases is five. The greatest number of significant cases was reached between nocturnal RMSSD and RRi from sitting phase.

Table 5: Mean of correlation coefficients, SWS segment

	RMSSD(1)	pNN50(1)	RRi(1)	RMSSD(2)	pNN50(2)	RRi(2)	HRs	TTL
RRi	0.16	0.19	0.12	0.15	0.18	0.14	0.03	0.08
	(0.24)	(0.20)	(0.15)	(0.23)	(0.29)	(0.25)	(0.20)	(0.26)
Std RRi	0.25	0.30	0.18	0.15	0.15	0.26	0.09	-0.07
	(0.18)	(0.20)	(0.14)	(0.20)	(0.19)	(0.26)	(0.21)	(0.16)
HF peak	0.00	0.02	0.06	-0.05	-0.09	0.11	0.02	0.05
	(0.27)	(0.23)	(0.29)	(0.13)	(0.17)	(0.27)	(0.18)	(0.20)
RMSSD	0.26	0.34	0.23	0.15	0.13	0.23	0.11	-0.04
	(0.17)	(0.24)	(0.16)	(0.22)	(0.23)	(0.26)	(0.23)	(0.15)
LF/HF	-0.00	0.01	-0.12	0.01	-0.01	-0.06	-0.02	0.07
	(0.25)	(0.28)	(0.29)	(0.18)	(0.22)	(0.33)	(0.26)	(0.17)
HFP	0.25	0.32	0.23	0.14	0.13	0.21	0.14	-0.05
	(0.19)	(0.23)	(0.14)	(0.25)	(0.25)	(0.26)	(0.25)	(0.19)
LFP	0.23	0.27	0.11	0.13	0.13	0.20	0.08	-0.06
	(0.20)	(0.20)	(0.16)	(0.22)	(0.15)	(0.27)	(0.20)	(0.15)
rRR	-0.06	-0.13	-0.14	-0.04	-0.03	-0.07	-0.03	0.00
	(0.23)	(0.22)	(0.23)	(0.16)	(0.20)	(0.28)	(0.22)	(0.17)
fIndex	0.11	0.10	0.04	0.09	0.15	0.02	-0.01	0.05
	(0.26)	(0.18)	(0.18)	(0.17)	(0.25)	(0.27)	(0.14)	(0.22)

Note: The variables marked with (1) represent orthostatic test in sitting phase and (2) respectively for standing phase. Rows with brackets represent the standard deviation of the coefficient above.

Table 6: The number of significant cases, SWS segment, ($N = 11$)

	RMSSD(1)	pNN50(1)	RRi(1)	RMSSD(2)	pNN50(2)	RRi(2)	HRs	TTL
RRi	5	3	0	3	4	2	0	2
Std RRi	5	6	3	2	2	8	1	0
HF peak	3	2	4	0	1	2	0	1
RMSSD	3	5	5	3	3	5	3	1
LF/HF	1	2	4	1	1	3	1	0
HFP	5	5	4	4	3	4	3	1
LFP	5	4	0	3	1	5	1	1
rRR	1	2	4	1	1	4	1	1
fIndex	3	1	1	0	2	3	0	2

Note: The variables marked with (1) represent orthostatic test in sitting position and (2) respectively for standing position.

Table 7: Mean of correlation coefficients, Evening segment

	RMSSD(1)	pNN50(1)	RRi(1)	RMSSD(2)	pNN50(2)	RRi(2)	HRs	TTL
RRi	0.06	0.06	0.22	0.08	0.09	0.12	0.06	0.01
	(0.24)	(0.24)	(0.28)	(0.20)	(0.29)	(0.34)	(0.22)	(0.28)
Std RRi	0.27	0.25	0.12	0.15	0.13	0.16	0.05	0.00
	(0.24)	(0.24)	(0.28)	(0.20)	(0.29)	(0.34)	(0.22)	(0.28)
HF peak	0.01	-0.02	-0.14	-0.07	-0.10	0.06	-0.13	0.10
	(0.22)	(0.19)	(0.24)	(0.19)	(0.30)	(0.24)	(0.28)	(0.28)
RMSSD	0.17	0.24	0.18	0.16	0.17	0.19	0.08	-0.02
	(0.21)	(0.20)	(0.30)	(0.23)	(0.19)	(0.33)	(0.11)	(0.12)
LF/HF	-0.14	-0.20	-0.19	-0.04	-0.05	-0.14	-0.14	0.17
	(0.22)	(0.23)	(0.23)	(0.23)	(0.24)	(0.34)	(0.21)	(0.17)
HFP	0.18	0.24	0.22	0.16	0.18	0.20	0.12	-0.04
	(0.20)	(0.19)	(0.30)	(0.24)	(0.22)	(0.39)	(0.14)	(0.14)
LFP	0.11	0.17	0.15	0.06	0.08	0.14	0.08	0.02
	(0.15)	(0.17)	(0.27)	(0.23)	(0.21)	(0.31)	(0.17)	(0.21)
rRR	-0.05	-0.16	-0.18	-0.03	-0.02	-0.14	-0.10	0.05
	(0.12)	(0.14)	(0.26)	(0.16)	(0.25)	(0.28)	(0.22)	(0.20)
fIndex	0.05	0.07	0.22	0.09	0.09	0.06	0.08	-0.02
	(0.21)	(0.22)	(0.22)	(0.21)	(0.30)	(0.31)	(0.17)	(0.27)

Note: The variables marked with (1) represent orthostatic test in sitting phase and (2) respectively for standing phase. Rows with brackets represent the standard deviation of the coefficient above.

Table 8: The number of significant cases, Evening segment, ($N = 11$)

	RMSSD(1)	pNN50(1)	RRi(1)	RMSSD(2)	pNN50(2)	RRi(2)	HRs	TTL
RRi	2	2	4	2	2	4	2	4
Std RRi	5	5	3	3	2	5	1	1
HF peak	2	0	4	0	2	2	4	4
RMSSD	3	4	7	3	2	5	0	0
LF/HF	1	4	3	2	3	5	2	2
HFP	3	5	6	4	4	5	1	0
LFP	0	3	3	2	1	5	1	1
rRR	0	1	3	0	1	4	3	1
fIndex	2	2	3	2	3	4	1	4

Note: The variables marked with (1) represent orthostatic test in sitting position and (2) respectively for standing position.

Summary

On the group level, there were significant differences between all the different conditions (the SWS segment, the Evening segment, the sitting phase and the standing phase) in mean RRi and RMSSD. The greatest number of significant correlations was found between the std RRi from the SWS segment and the mean RRi from the standing phase of the orthostatic test. There was significance in $\frac{8}{11}$ cases. According to the correlation analysis, the result of std RRi and standing RRi could be interpreted in a way that when ones standing RRi in an orthostatic test is low, the RRi is also more stable during slow-wave sleep. This stability could be caused by parasympathetic withdrawal. The decreased standing RRi could be caused by enhanced sympathetic activity. The findings from the SWS segment should be further verified with a sleep study where sleep phases would be verified via polysomnographic measurement.

The second largest number of significant cases was found between the RMSSD from the Evening segment and the mean RRi from the sitting phase of the orthostatic test. There were significance in $\frac{7}{11}$ cases. On average, the correlation was positive which could be interpreted as follows: when one has high RMSSD during SWS segment, then the mean RRi during the sitting phase of the orthostatic test is also slightly higher. An increase in RRi and RMSSD values are both caused by an increase in parasympathetic activity. This points out that there are some similarities in nocturnal parasympathetic activity and the parasympathetic activity in the sitting phase of the orthostatic test.

5 Conclusions

The analysis of the level of fatigue from nocturnal HRV was recognized to be rather difficult. In order to prevent overtraining, it is of paramount importance to be able to monitor one's training load and stress.

The group level results show that the ANS activity is different during sleep from the ANS activity during wake. The individual level results give an indication that the nocturnal RMSSD (evening segment) and the nocturnal standard deviation of RRi (SWS segment) could possibly be used in evaluating fatigue at some point, but not until further research has been performed. In further studies, these two variables should be examined in a proper overtraining study. That would reveal the true ability of these two variables to detect fatigue.

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